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## Alexithymia and pain experience among patients using methadone-maintenance therapy

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### Abstract

**Background:** Alexithymia, difficulty identifying and describing one's emotions coupled with a tendency to externalize, is a potentially important yet understudied treatment target for patients with opioid use disorder. The aim of this study was to examine the role of alexithymia in pain experience among individuals with opioid use disorder.

**Methods:** One-hundred-and-sixty-four patients receiving methadone maintenance treatment completed a battery of self-report measures related to alexithymia, drug use, and pain experiences. Comparisons were performed on the full sample between those with or without clinically significant levels of alexithymia. For a subsample reporting pain ( $n = 138$ ), intercorrelations were performed to test whether drug use history, pain catastrophizing, pain acceptance, and alexithymia were related to pain severity and pain interference. Regression analyses were performed to test for serial mediation of pain catastrophizing and pain acceptance on the relationship between alexithymia and pain interference in this subsample.

**Results:** Individuals with alexithymia showed increased pain catastrophizing and interference, and intercorrelations indicated that increased alexithymia was associated with increased pain

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Contributors

Drs. Barry and Beitel conceived of, and implemented, the initial study. Dr. Morie wrote the first draft of the paper and worked with co-authors on subsequent drafts. All authors contributed to the editorial process and have approved the final submitted version of the manuscript.

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interference, more pain catastrophizing, and reduced pain acceptance. A serial regression model among a subset of patients with pain indicated that pain catastrophizing and pain acceptance mediated the effect of alexithymia on pain interference.

**Conclusions:** These findings suggest that alexithymia, as well as both pain catastrophizing and pain acceptance, contribute to interference associated with pain and are potentially important intervention targets among methadone-treated patients with pain.

## Keywords

Alexithymia; Opioid Use Disorder; Methadone; Pain

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## 1. Introduction

Methadone maintenance treatment (MMT) is a first-line, evidence-based treatment for opioid use disorder (OUD) that decreases opioid overdose, hepatitis C and HIV, all-cause mortality, and illegal activities (Association of Schools and Programs of Public Health, 2019; National Academies of Sciences, 2019). MMT accounts for approximately 21–25% of treatment admissions for OUD each year (Alderks, 2013) and consists of methadone, an FDA-approved opioid agonist medication, usually accompanied by a psychosocial treatment (Office of National Drug Control Policy, 2012; Pecoraro et al., 2012).

Alexithymia, or difficulties identifying and describing one's emotions coupled with tendencies to externalize (Parker, 2003), may interfere with emotional self-disclosure, a cornerstone of many psychosocial treatments (Lumley, 2004). Alexithymia is commonly considered a personality trait and exists along a continuum; however, research instruments such as the Toronto Alexithymia Scale have established cut-offs for clinically elevated scores (Bagby et al., 1994). Genetic factors including polymorphisms in *DRD2/ANKK1* and *BDNF* (Walter et al., 2011) and reductions in anterior cingulate volumes (Berthoz et al., 2002) have been implicated in alexithymia. Alexithymia is common in individuals with chronic pain (Di Tella and Castelli, 2016) and is specifically linked to pain experiences (Nyklicek and Vingerhoets, 2000; Shibata et al., 2014). While alexithymia has been examined among individuals with substance use (de Haan et al., 2014) and substance use disorders (Cleland et al., 2005; Ghalehban and Besharat, 2011; Haviland et al., 1994), no studies to our knowledge have systematically examined the prevalence and correlates of alexithymia among patients receiving MMT, especially among individuals with chronic pain (i.e., non-cancer pain lasting at least 3 months), a particularly vulnerable clinical group (Dhingra et al., 2013).

Estimates of chronic pain among patients in MMT vary between 37% to over 60% (Jamison et al., 2000; Peles et al., 2005; Rosenblum et al., 2003). MMT patients with chronic pain report higher levels of psychiatric comorbidity compared with their counterparts without pain (Barry et al., 2011; Higgins et al., 2020; Rosenblum et al., 2003). Studies of individuals without SUDs have found that pain catastrophizing, pain acceptance, and alexithymia are related to the experience of pain. Pain catastrophizing includes pain-related magnification, helplessness, and rumination (Sullivan et al., 1995), worsens treatment outcomes (Quartana et al., 2009), and is robustly associated with higher pain intensity and interference in

functioning associated with pain (i.e., pain interference) (Severeijns et al., 2001). Pain acceptance refers to learning to live with one's pain and is considered an adaptive strategy for pain management, improving treatment outcomes. Pain acceptance is associated with lower pain intensity and interference (McCracken, 1998; McCracken et al., 2004; Mun et al., 2019). Prior research about MMT patients with pain has found that pain catastrophizing is associated with pain intensity and pain-related disability (Garnet et al., 2011). In a previous study with the current patient population, (Mun et al., 2019), we found pain acceptance and catastrophizing were associated with both pain intensity and pain interference. However, we did not examine alexithymia or its association with pain intensity, interference, catastrophizing, or acceptance.

Although little research has examined alexithymia in methadone-maintained individuals with chronic pain, several lines of evidence suggest clinically relevant interactions between pain, alexithymia and OUD symptoms. For example, alexithymia has been positively associated with OUD symptoms and nonmedical prescription use in patients on long-term opioid therapy for chronic pain (Oberleitner et al., 2019). Alexithymia is also associated with increased prescription opioid use and poorer outcomes (persistent pain intensity and disability) among individuals with chronic pain (Saariaho et al., 2017). Previous examinations of alexithymia and pain catastrophizing have suggested that catastrophizing mediates the relationship between alexithymia and pain interference in individuals with chronic headaches (Shim et al., 2018) and asthma (Ghorbani et al., 2017). However, the relationship between alexithymia and pain interference (a key target of psychosocial treatments for chronic pain) among MMT patients with pain is unclear, as are the possible mediating effects of both pain catastrophizing and acceptance on this relationship. Difficulties identifying and understanding emotions related to pain may result in a tendency to misinterpret negative emotional arousal in the body as physical pain and to hyper-focus on the physical experience of pain. Both tendencies may lead to perceiving pain as increasingly uncontrollable, anxiety-inducing, and overwhelming, which may promote catastrophizing and diminish pain acceptance. Thus, alexithymia may be an underlying vulnerability factor that worsens pain interference among MMT patients with pain.

Given the gaps in the literature on the role of alexithymia in MMT patients and their pain experiences, this study had several aims. First, to examine alexithymia in individuals with OUD receiving MMT in order to investigate the relationship between alexithymia and OUD-related characteristics, including years of opioid use, age of initiation of heavy opioid use, and pain associated with withdrawal. We hypothesized that alexithymia would be associated with aspects of substance use history, including more years of opioid use and a younger age of initiation of heavy opioid use. The second aim was to examine relationships between alexithymia and pain experiences, including pain catastrophizing, acceptance, intensity, and interference. This aim focused upon a subset of the sample of patients who reported pain. We hypothesized that alexithymia would be positively correlated with pain catastrophizing and negatively with pain acceptance, and through pain catastrophizing and acceptance, lead to greater pain interference.

## 2. Methods

### 2.1 Setting

This study was conducted at the Addiction Prevention and Treatment (APT) Foundation, a community-based not-for-profit organization headquartered in a mid-sized city in New England with a census of approximately 4,500 MMT patients<sup>1</sup>. The APT Foundation provides eligible patients with OUD access to methadone on the same day as screening, irrespective of ability to pay, and patients are provided access to a variety of group and individual counseling options from which they are free to choose (Madden et al., 2018).

### 2.2 Participants

The full sample of participants consisted of 164 individuals enrolled in MMT at the APT Foundation (APT). As part of admission into MMT at APT, all participants met with a master's level clinician who confirmed they met Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) criteria for OUD. For examination of pain-related measures, we focused upon a subset of 138 participants who reported some or chronic pain.

### 2.3 Procedures

The study, involving the use of survey data without identifiers, was approved by the APT Foundation Board and was presented to the Institutional Review Board at a local medical school affiliated with APT, which exempted it from review. Participants were recruited between January 2014 and March 2015 by fliers posted at three of APT's MMT clinics. The fliers stated, "Want to help us improve methadone treatment? Tell us about your experiences at APT Foundation!" Study eligibility included current receipt of MMT at an APT clinic and English proficiency. Research assistants administered the questionnaire packet after describing the study. All patients who met with the research assistant completed the study. Participants were compensated \$15 for their study participation. Participants' mean age was 43.8 years (SD = 10.8), and 59% of the sample was male.

### 2.4 Measures

**2.4.1 Alexithymia**—The 20-item Toronto Alexithymia Scale (TAS-20) (Bagby et al., 1994) was used to measure alexithymia. Items are rated using a 5-point Likert scale whereby 1 = strongly disagree and 5 = strongly agree (e.g., "I have feelings that I can't quite identify"). Subscales of the TAS-20 include difficulty identifying feelings, difficulty describing feelings, and externalization. A cut-off score of 61 is typically used to indicate clinically meaningful alexithymia (Bagby et al., 1994). We used the total score with higher scores indicating greater alexithymia. Cronbach's alpha was .86.

**2.4.2 Pain Intensity**—We measured pain intensity with the Brief Pain Inventory (BPI) (Cleeland and Ryan, 1994). It is based upon 0 to 10 Numerical Rating Scales. A composite of four items ("average," "worst," and "least" pain past in the past 7 days, and pain "right

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<sup>1</sup>36% female with a mean age of 37 (SD=11); 80% self-identify as Caucasian, 10% as Latinx, 8% as Black, and 2% as "Other"

now”) (e.g., “Please rate your pain by circling the number that best describes your pain at its worst in the past week”). Previous studies demonstrated that these four items load well together on a single factor (Caraceni et al., 1996; Cleeland and Ryan, 1994; Ger et al., 1999; Radbruch et al., 1999; Wang et al., 1996). Cronbach’s alpha was .78.

**2.4.3 Pain Interference**—Pain interference was measured via the composite (mean) of seven BPI items assessing the extent to which patients considered that pain interfered with their (1) general activity, (2) relationships with other people, (3) mood, (4) sleep, (5) work, (6) walking, and (7) enjoyment of life over the past 7 days. Previous factor analyses found that these items indicating pain interference load together on a single factor (Caraceni et al., 1996; Cleeland and Ryan, 1994; Ger et al., 1999; Radbruch et al., 1999; Wang et al., 1996). Cronbach’s alpha was .87.

**2.4.4 Pain Catastrophizing**—Pain catastrophizing was measured by the 13-item Pain Catastrophizing Scale (PCS) (Sullivan et al., 1995). Each item is rated on a scale from 0 = not at all to 4 = all the time and assesses the extent to which participants tend to feel helpless, magnify, and ruminate about their pain experience. We used the total score, with higher scores indicating greater pain catastrophizing. Total PCS scores above 30 indicate clinically meaningful levels of pain catastrophizing (Sullivan et al., 1995). Cronbach’s alpha was .93.

**2.4.5 Pain Acceptance**—The 20-item Chronic Pain Acceptance Questionnaire (CPAQ-20) (McCracken et al., 2004) was used to measure the extent to which individuals are willing to engage in important daily activities despite experiencing pain while not trying to avoid or control their pain. Each of the items is rated on a scale from 0 = never true to 5 = always true. We used the total score with higher scores indicating greater pain acceptance. Cronbach’s alpha was .70.

## 2.6 Statistical analyses

Data analysis was performed in IBM SPSS Statistics version 26. To fulfill our first aim, comparisons were performed on the full sample ( $N = 164$ ) between individuals with ( $n = 61$ ) and without ( $n = 103$ ) clinically significant alexithymia, using the cut-off score of 61 on the TAS-20. We used t-tests for continuous variables and chi-square tests for dichotomous variables. Correlations were performed between all 164 participants for alexithymia and methadone dose, years of opioid use, and age of onset of heavy opioid use.

Consistent with prior research on pain classification (Barry et al., 2009; Rosenblum et al., 2003), 138 individuals were identified who reported “some” (i.e., pain reported in the past week but not chronic pain) or “chronic” pain (i.e., pain lasting at least 6 months with a score of 5 or higher on the BPI item pertaining to the typical level of pain intensity in the last 7 days or on any of the BPI items relating to pain interference in the last 7 days)<sup>2</sup>. To fulfill the goals of our second aim, comparisons between those with high ( $n = 57$ ) and low ( $n = 81$ ) alexithymia for pain-related measures were performed between the 138 individuals who

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<sup>2</sup>We used a conservative definition of chronic pain.

reported some or chronic pain, and are included in Table 1b. Additionally, correlations were calculated in this sub-sample between scores on the TAS-20, pain catastrophizing, pain interference, pain intensity, and pain acceptance, and are shown in Table 2.

To construct the serial mediation model, we followed previously established criteria (Hayes, 2013; Hayes and Matthes, 2009), and included only the 138 individuals who reported pain. Criteria require that the causal variable in the mediation model must be correlated both with the outcome variable and with the mediator. Thus, factors with significant intercorrelations were subsequently entered into the serial mediation model.

Scores on the TAS-20, BPI pain interference, and the PCS and the CPAQ were entered respectively as independent, dependent, and mediator variables. The model was tested using SPSS PROCESS (Hayes, 2013), which utilizes bootstrapping. Significance was set at  $p = 0.05$  and when 95% CI did not include zero. The serial mediation analysis utilized the default model 6 embedded within SPSS PROCESS (Hayes and Matthes, 2009) to examine the direct path between alexithymia and pain interference and the potential indirect paths through pain catastrophizing and pain acceptance. We did not modify for additional paths in the mediation model. The data also met the assumptions of linearity, homogeneity of error variance, and multicollinearity (All VIF values  $< 2$ ). Skewness for all variables was within  $\pm 9$  and kurtosis for all variables was within  $\pm 1.5$ . We also examined this model in a subset of 78 individuals who reported chronic pain as a sensitivity analysis, and these data are included in supplementary materials.

**2.6.1 Covariates**—The following variables were included as covariates in the regression analyses. *Gender.* Participant gender (male or female) was self-reported. Other categories (e.g., intersex, transgender) were not included. Females generally report more severe pain symptoms (Bartley and Fillingim, 2013).

**Age.:** Participants reported their age when completing survey questionnaires. Older individuals may report more severe pain (Andersson et al., 1993).

**Race.:** Participants were asked to report their race based upon categories including white, black, Native American, Asian American, and other. As few participants self-identified as being of a race other than white or black (see Table 1), we collapsed all racial minority categories into one. Hence, when using the race as a covariate in main analyses, we coded 0 as white and 1 as racial/ethnic minority. Some studies suggest that individuals from racial minority versus racial majority groups may experience more pain symptoms (Shavers et al., 2010).

**Current Methadone Dose (mg/day).:** Participants' responses to the question, "What is your current methadone dose?" were used to define current methadone doses (mg/day). Individuals who take higher doses of methadone may experience more pain severity, potentially due to increased pain sensitivity as a result of opiate use (Peles et al., 2005).

### 3. Results

#### 3.1 Participant characteristics: Demographics, pain, drug use behavior and alexithymia

Of the sample of 164 patients receiving MMT, 78 individuals reported chronic pain, 60 reported some pain, and 26 reported no pain in the past week and no chronic pain (“no pain”). For the initial analysis on drug use behavior, we divided participants into high and low alexithymia groups based upon their total TAS-20 score. Thirty-seven percent of the sample exhibited clinical levels of alexithymia based on the cutoff score (N= 61; alexithymia group), and the remainder was low in alexithymia (N=103). There were no differences between alexithymia groups for any measure of drug use behavior, including years of opioid use, age at initiation of heavy opioid use, or methadone dose (all p values > .2). Patients varied in duration of MMT from 0.25 to 300 months (M=41.1, SD = 53.1). Duration of MMT was not significantly associated with the total score on the TAS ( $r=0.002$ ,  $p = 0.98$ ). Detailed demographic information is presented in Table 1a. We further divided those participants who reported some or chronic pain into high (n= 57) and low (n= 81) alexithymia groups to examine pain-related measures.

Individuals in the alexithymia group reported lower pain acceptance ( $F_{1,136} = 9.9$ ,  $p < .001$ ,  $\eta^2 = .07$ ), lower pain willingness on the CPAQ scale ( $F_{1,136} = 11.42$ ,  $p < .001$ ,  $\eta^2 = .07$ ), higher pain magnification scores ( $F_{1,136} = 15.64$ ,  $p < .001$ ,  $\eta^2 = .10$ ) and more pain rumination ( $F_{1,136} = 12.89$ ,  $p < .001$ ,  $\eta^2 = .08$ ), and increased interference due to pain ( $F_{1,136} = 17.69$ ,  $p < .001$ ,  $\eta^2 = .11$ ). However, there were no differences in pain intensity ( $F_{1,136} = 1.11$ ,  $p = .29$ ,  $\eta^2 = .002$ ) or duration of pain ( $F_{1,136} = .21$ ,  $p = .64$ ,  $\eta^2 = .002$ ) between individuals high and low in alexithymia. Detailed pain-related information is presented in Table 1b.

#### 3.2 Correlations between alexithymia, pain experiences, and drug use

In bivariate analyses in the full sample of 164 individuals, alexithymia (total score on the TAS-20) was not associated with indices of drug use, including years of opioid use ( $r = -.12$ ,  $p = .14$ ), age of first use ( $r = .12$ ,  $p = .13$ ), or methadone dose ( $r = .002$ ,  $p = .98$ ). In the 138 individuals who reported pain, alexithymia (total score on the TAS-20) was positively associated with measures of rumination ( $r = .34$ ,  $p < .01$ ), magnification ( $r = .41$ ,  $p < .01$ ), pain catastrophizing ( $r = .43$ ,  $p < .01$ ) and pain interference ( $r = .35$ ,  $p < .01$ ). Alexithymia was negatively associated with pain acceptance ( $r = -.26$ ,  $p < .01$ ). Correlations for this sample of 138 participants are reported in table 2.

#### 3.3. Regression models: Alexithymia and pain interference

We examined a serial mediation model (Figure 1) that tested for the mediating effects of pain catastrophizing and pain acceptance on the relationship between alexithymia and pain interference in the 138 individuals who reported pain.

Results of serial multiple mediation analysis of the pathway between alexithymia and pain interference through pain catastrophizing and pain acceptance, while controlling for gender, methadone dose, ethnicity, and age, are shown in Figure 1. The direct and indirect effects are described below.

Alexithymia was associated with greater pain catastrophizing ( $b=6.74$ ,  $se=1.29$ ,  $p<.001$ ) and accounted for significant variance in catastrophizing ( $R^2=.22$ ,  $F(5,126)=7.43$ ,  $p=.000$ ). Racial/ethnic minority status was also associated with greater pain catastrophizing ( $b=2.5$ ,  $se=1.1$ ,  $p<.03$ ).

Pain catastrophizing ( $b=-.59$ ,  $se=.08$ ,  $p<.001$ ), but not alexithymia ( $b=-.8$ ,  $se= 1.3$ ,  $p=.55$ ), was associated with less pain acceptance and accounted for significant variance in pain acceptance ( $R^2=.37$ ,  $F(6,125)=12.27$ ,  $p<.001$ ). No covariates were associated with pain acceptance (all  $p$  values  $> .05$ ).

Alexithymia was not associated directly with pain interference ( $b=.23$ ,  $se= .19$ ,  $p=.23$ ), but both pain catastrophizing ( $b=.06$ ,  $se= .01$ ,  $p<.0001$ ) and pain acceptance ( $b=-.05$ ,  $se= .01$ ,  $p=.001$ ) were and accounted for significant variance in pain interference ( $R^2=.73$ ,  $F(7,124)=20.44$ ,  $p<.001$ ). Female gender was also significantly associated with greater pain interference ( $b=1.07$ ,  $se= .30$ ,  $p<.001$ ).

The indirect effect of alexithymia on pain interference, individually through pain catastrophizing, was significant ( $b=.46$ ,  $se=.16$ ,  $95\%CI=.40, 1.06$ ), though the indirect effect of alexithymia on pain interference through pain acceptance was not ( $b=.04$   $se=.06$ ,  $95\%CI=-.09, .17$ ). However, the serial double indirect effect of alexithymia, through pain catastrophizing and pain acceptance, on pain interference was significant ( $b=.20$ ,  $se=.07$ ,  $95\%CI=.07, .36$ ), indicating that alexithymia was associated with greater pain catastrophizing, which in turn was associated with less pain acceptance, which in turn was associated with greater pain interference.

#### 4. Discussion

This study examined two aims. We first examined the prevalence and correlates of alexithymia in a sample of MMT patients. Additionally, we examined alexithymia in a subsample reporting pain and used serial mediation modeling to identify indirect effects of alexithymia on pain interference via pain catastrophizing and pain acceptance. Of the total sample, over a third reported clinically significant alexithymia, and individuals with alexithymia reported more pain catastrophizing, more pain interference, and less pain acceptance, although pain intensity and duration of pain were similar across alexithymia groups. Among those with some or chronic pain, alexithymia and pain catastrophizing were strongly and positively correlated, with large effect sizes for both the total catastrophizing score and the rumination and magnification subscales of the catastrophizing scale, while alexithymia and pain acceptance were highly negatively correlated. Further investigations using a regression model indicated that the relationship between alexithymia and pain interference may be mediated by pain catastrophizing through pain acceptance, and this held true for both individuals with some or chronic pain as reported in supplementary materials. No relationships between drug use history and pain or alexithymia measures were seen in our analyses, though individuals with alexithymia were more likely to report pain due to opioid withdrawal.



These findings replicate previous work related to pain experience and OUD (Mun et al., 2019), while extending them to consider alexithymia, in a serial mediation model. The prevalence of alexithymia in this sample with OUD was comparable to previous examinations of alexithymia in patients who misused substances (Haviland et al., 1994), which indicated that 41% of individuals hospitalized for SUDs exhibited clinically significant alexithymia. It is also comparable to frequencies of alexithymia seen in a previous examination of methadone-maintained individuals, although participants in that study were also being treated for cocaine-use disorder (Morie et al., 2015).

Alexithymia was associated with pain interference, but not with pain intensity, suggesting alexithymia may contribute to the experience of how pain interferes with daily life, but not the actual physical sensation. This is somewhat inconsistent with reports demonstrating a relationship between alexithymia and pain intensity (Aaron et al., 2019; Di Tella and Castelli, 2016; Shibata et al., 2014). It is possible that differences in study populations may explain this apparent discrepancy.

The presence of alexithymia coupled with chronic pain may worsen pain interference as emotions related to pain experience may be harder for those with alexithymia to identify and thus regulate (Kano and Fukudo, 2013). This could underlie the relationship we observed between elements of pain catastrophizing, including increased pain magnification and rumination, and alexithymia. The relationship between pain catastrophizing and pain interference is well-characterized (Hanley et al., 2008; Mun et al., 2019), as is the relationship between alexithymia and pain interference (Shibata et al., 2014). Our findings, specifically the mediation analysis between alexithymia, catastrophizing, pain acceptance and pain interference, suggest alexithymia may contribute to increased catastrophizing, to decreased acceptance, and thus to further pain interference, and is consistent with findings on alexithymia and pain catastrophizing in individuals without OUD who have chronic pain (Vargovich et al., 2015). Few studies have expressly examined pain acceptance and alexithymia, though investigations into the related concept of self-efficacy have found that it similarly moderates the relationship between alexithymia and pain intensity (Mirjalili et al., 2011). External barriers may hinder the development of pain acceptance, including obtaining a diagnosis and one's peers recognizing the pain as real (Lachapelle et al., 2008). Alexithymia may exist as an internal barrier that potential treatments could target.

Our findings illustrate that alexithymia is an important characteristic closely associated with pain interference, and its effects are mediated by catastrophizing and reduced pain acceptance. Alexithymia has also been a relevant factor in treatment success among patients in MMT with cocaine use disorder (Morie et al., 2015). Treatments addressing pain experience in OUD, however, do not typically address alexithymia. Pharmacotherapy is sometimes used to address pain in MMT settings (Alford, 2013) but few integrated psychosocial treatments exist for addressing co-occurring chronic pain and OUD (Barry et al., 2019; Garland et al., 2019). Psychological treatments centered on recognition and processing of emotion may be effective in reducing both alexithymia and depressive symptoms in individuals with chronic pain (Melin et al., 2010). Such treatments may also benefit patients with OUD and chronic pain since they frequently experience depression (Barry et al., 2016; Higgins et al., 2019). Although the development of psychosocial

treatments to specifically address alexithymia among patients with opioid use disorder and chronic pain is still in its infancy, some approaches such as mindfulness training (Norman et al., 2019) and emotional awareness therapy (Lumley and Schubiner, 2019) hold promise. Future work on the development of integrated treatment approaches for OUD and chronic pain should address alexithymia and pain-related characteristics.

A null finding in this study for the relationship between alexithymia and drug use history was somewhat surprising given previous reported links between these variables (de Haan et al., 2014). Differences in study measures and patient populations may account for this apparent inconsistency. It should be noted, however, that while alexithymia is common among individuals who use drugs (Evren et al., 2008; Ghalehban and Besharat, 2011), it is not always related to severity of use (Pinard et al., 1996; Thorberg et al., 2009), and this topic merits further investigation. Future research should consider examining longitudinally relationships between alexithymia, drug use, distress tolerance, and retention in MMT.

#### 4.1 Limitations

Findings should be considered with respect to limitations. The data for the PCS variable were not normally distributed, which is not a limitation for regression analyses but may limit interpretation for between-group comparisons. Recruiting a relatively small convenience sample from a not-for-profit organization in New England may limit the study's generalizability to MMT programs with different treatment models or in other regions. Data were cross-sectional and causal inferences cannot be drawn. The cross-sectional information also weakens the potential impact of our mediation analyses. However, theoretical links between alexithymia and pain catastrophizing, acceptance, and interference are strong and consistent with previous longitudinal studies. While study variables were correlated with each other as a prerequisite for mediation modeling, there was no evidence of multicollinearity in the model. Another limitation is data on the onset of OUD and chronic pain were unavailable. Future research on pain in OUD populations would benefit from these data. Finally, data on concurrent use of illicit opioids and other substances, including tobacco, alcohol, and cannabis, were not collected, precluding information on their potential influence on pain experience and alexithymia.

#### 4.2 Conclusions

A serial mediation illustrated the relationship between alexithymia and pain interference that was mediated by both pain catastrophizing and pain acceptance and supported our proposed model of how alexithymia may contribute to pain interference. Our findings illustrate the important role of alexithymia in the relationships between pain catastrophizing, acceptance, and interference in MMT populations, and suggest alexithymia as a potential treatment target.

### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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### Conflicts of Interest

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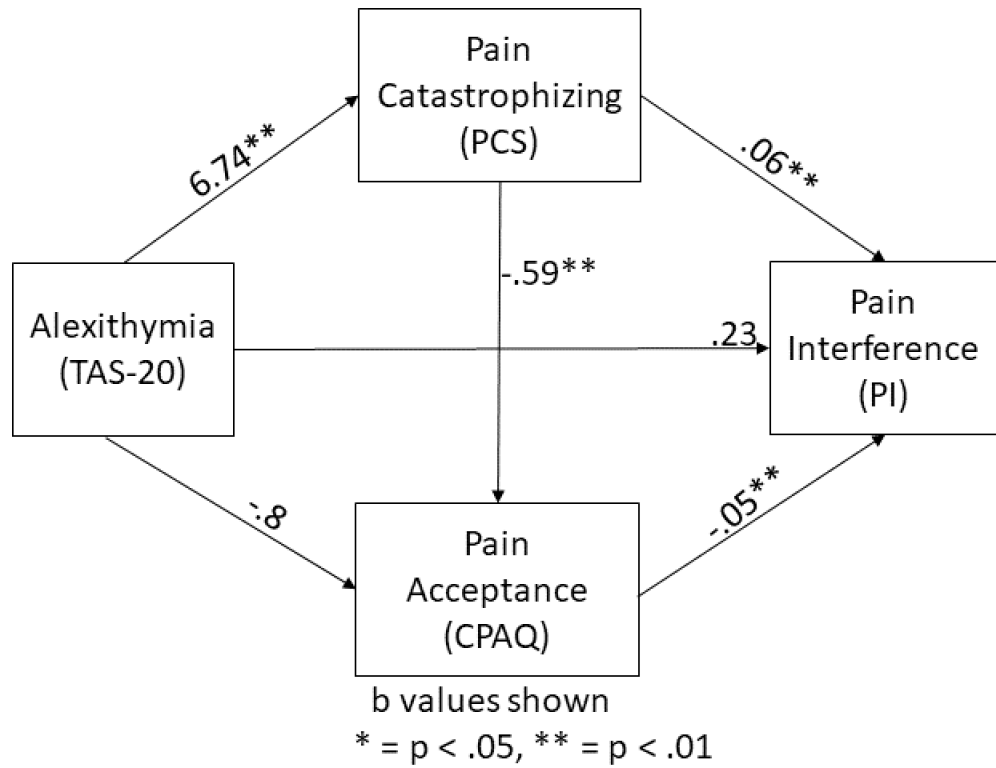
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### Highlights

- We explored alexithymia and pain in patients in treatment for opioid use disorder.
- Alexithymia was associated with greater pain interference and pain catastrophizing.
- Increased alexithymia was associated with reduced pain acceptance.
- Alexithymia contributes to pain interference and may be a therapeutic target.
- Pain catastrophizing and acceptance mediated effects of alexithymia on interference.



**Indirect b values**

TAS-20 → PCS → PI: .46\*

TAS-20 → CPAQ → PI: .04

TAS-20 → PCS → CPAQ → PI: .20\*

**Figure 1:** Serial mediation model: Alexithymia, pain interference, and the mediating effects of pain catastrophizing and acceptance in individuals with some or chronic pain (N = 138).



**Table 1a:**

Comparison of demographic information between individuals high and low in alexithymia across the full sample of 164 patients receiving MMT.

	<u>Low ALX (N = 103)</u>		<u>High ALX (N = 61)</u>		<u>Total (N = 164)</u>		f	p
	mean	sd	mean	sd	mean	sd		
Age	43.87	10.66	43.92	10.10	43.89	10.45	0.00	0.97
Height (inches)	67.27	4.09	67.87	4.07	67.49	4.08	0.84	0.36
Weight (lbs)	178.26	46.40	187.45	47.20	181.68	46.77	1.48	0.22
Age opiate Initiation	23.90	7.60	23.36	9.85	23.70	8.51	0.15	0.70
Methadone Dose	81.80	29.60	75.67	31.78	79.52	30.53	1.54	0.21
Years of opiate use	19.08	11.91	18.58	10.40	18.90	11.30		
	#	%	#	%	#	%	$\chi$	p
<b>Gender</b>							0.87	0.44
<i>Male</i>	60.00	58.00	37.00	60.00	97.00	59.00		
<i>Female</i>	43.00	42.00	24.00	40.00	67.00	41.00		
<b>Education Completed</b>							8.20	0.31
<i>Grades 6–8</i>	2.00	1.00	4.00	6.00	6.00	4.00		
<i>Some High School</i>	18.00	18.00	15.00	25.00	33.00	20.00		
<i>HS/GED</i>	46.00	45.00	28.00	44.00	74.00	45.00		
<i>Some College</i>	19.00	19.00	7.00	11.00	26.00	16.00		
<i>Associate's Degree</i>	6.00	6.00	2.00	3.00	8.00	5.00		
<i>Bachelor's Degree</i>	2.00	1.00	3.00	5.00	5.00	3.00		
<i>Some vocational training</i>	6.00	6.00	1.00	2.00	7.00	4.00		
<i>Vocational Training</i>	4.00	4.00	1.00	2.00	5.00	3.00		
<b>Race</b>							4.90	0.29
<i>Black/AA</i>	30.00	29.00	18.00	28.00	48.00			
<i>White</i>	63.00	61.00	33.00	59.00	96.00			
<i>Asian or Pacific Islander</i>	2.00	3.00	0.00	0.00	2.00			
<i>American Indian/Alaska Native</i>	2.00	3.00	0.00	0.00	2.00			
<i>Other</i>	4.00	4.00	6.00	13.00	10.00			

**Table 1b:**

Comparison of pain-related information between individuals high and low in alexithymia in a subset of 138 individuals who reported some or chronic pain.

	Pain Group Only						f	p
	Low ALX (n = 81)		High ALX (n = 57)		Total (n = 138)			
	mean	sd	mean	sd	mean	sd		
Current Pain Duration (months)	46.77	76.94	40.91	54.39	44.27	68.02	0.21	0.64
<b>CPAQ Total Score</b>	59.29	14.39	51.71	13.22	56.16	14.37	9.90	0.00
CPAQ Activity Engagement	38.74	10.40	36.68	12.32	37.89	11.24	1.12	0.29
<b>CPAQ Pain Willingness</b>	20.55	10.24	15.03	8.10	18.27	9.80	11.42	0.00
<b>PCS Rumination Score</b>	8.93	4.65	11.82	4.64	10.13	4.84	12.89	0.00
<b>PCS Magnification Score</b>	5.66	3.63	8.12	3.53	6.68	3.77	15.64	0.00
Pain intensity	4.78	1.84	5.12	1.86	4.92	1.85	1.11	0.29
<b>Pain interference</b>	4.46	2.45	6.11	1.91	5.14	2.38	17.96	0.00
<b>PCS total</b>	22.83	11.95	33.49	13.56	27.23	13.65	23.81	0.00

ALX = Alexithymia; CPAQ = Chronic Pain Acceptance Questionnaire; PCS = Pain Catastrophizing Score

**Table 2:**

Intercorrelations for individuals with some or chronic pain (N = 138).

	1	2	3	4	5	6	7
<b>TAS-20 Total</b>							
1 Score	1	.34**	.41**	.43**	-.026**	0.10	.35**
2 PCS rumination Score		1.00	.80**	.92**	-.58**	.39**	.59**
3 PCS magnification Score			1.00	.91**	-.46**	.33**	.54**
4 PCS total score				1.00	-.60**	.39**	.65**
5 CPAQ total Score					1.00	-.36**	-.61**
6 Pain intensity						1.00	.49**
7 Pain interference							1.00

r values shown.

\* = p &lt; .05

\*\* = p &lt; .01.

ALX = Alexithymia; CPAQ = Chronic Pain Acceptance Questionnaire; PCS = Pain Catastrophizing Score